

---

(12) UK Patent Application (19) GB (11) 2 026 319 A

---

(21) Application No 7831555

(22) Date of filing

28 Jul 1978

(23) Claims filed

28 Jul 1978

(43) Application published

6 Feb 1980

(51) INT CL<sup>3</sup> A61K 31/07

7/48

(52) Domestic classification

A5B 170 26Y 343 34Y

360 36Y 38Y 39X J

(56) Documents cited

GB 1489133

The Theory and Practice  
of Industrial Pharmacy  
Lachman Lieberman and  
Kanig 2nd Edt 1976 pp  
184-243

(58) Field of search

A5B

(71) Applicant

Beecham Group Limited  
Beecham House  
Great West Road  
Brentford  
Middlesex TW8 9BD  
England

(72) Inventors

Inez Bowley

Raymond Guy Harrison

(74) Agents

Mr A J Walls

(54) Retinol acetate compositions

(57) A skin-care composition, effective in promoting epidermal mitosis, comprising from 20-40% by weight of oil, a non-ionic emulsifying agent in an amount greater than 1% by weight and retinol acetate in an amount from 1,000 to 15,000 IUg<sup>-1</sup>. The composition preferably contains butylated hydroxytoluene or butylated hydroxyanisole as an antioxidant.

BEST AVAILABLE COPY

GB 2 026 319 A

## SPECIFICATION

## Retinol acetate skin-care compositions

- 5 This invention relates to topical compositions containing vitamin A acetate, such compositions being of value in the care of the skin, and being specially formulated for maximum effectiveness. 5
- British Patent specification 1,489,133 describes and claims a liquid, semi-liquid or gel composition comprising a topically acceptable oil-in-water or water-in-oil emulsion base and  
 10 retinol acetate in an amount from 1,000 to 15,000 IUg<sup>-1</sup>, preferably 1,000 to 10,000 and more preferably 1,000 to 2,500 IUg<sup>-1</sup>. Such compositions are of value in promoting epidermal mitosis and thus lead to a desirable thickening or "plumping" effect on the skin. 10
- It has now been found that careful formulation of the emulsion base can lead to an unexpected increase in the effectiveness of the retinol acetate composition, resulting in high  
 15 activity in skin thickening or "plumping". 15
- Accordingly, the present invention provides a skin-care composition comprising an oil-in-water emulsion base comprising from 20-40% by weight of oil, a non-ionic emulsifying agent in an amount greater than 1% by weight and retinol acetate in an amount from 1,000 to 15,000 IUg<sup>-1</sup> preferably 3,000 to 6,900 IUg<sup>-1</sup>.
- 20 It is important for maximum effectiveness that the emulsion be oil-in-water rather than water-in-oil, since tests have shown that for a given concentration of retinol acetate and similar concentration of oil (sometimes called emollient) the former produces a greater degree of epidermal thickening. 20
- Moreover, it has been found that the effectiveness of the retinol acetate oil-in-water emulsion  
 25 is greatest with oil concentrations in the range 20-40%. Thus, emulsions with oil concentrations of about 10% and about 50% oil were less effective than otherwise identical emulsions containing about 30% oil. 25
- The further critical factor in optimising the effectiveness of the compositions of British Patent 1,489,133 has been found to be the choice of emulsifier type. In order of their ability to  
 30 produce skin thickening effect, anionic emulsifiers are less effective than non-ionic emulsifiers which in turn are less effective than cationic emulsifiers. However, the latter can cause skin irritation when embodied in retinol acetate compositions and are, therefore, not suitable. 30
- It has been found that the proportion of non-ionic emulsifier in the compositions of the invention is not critical, except that at least 1% by weight is required to give a stable emulsion.  
 35 However, an amount in the range 2% to 12%, preferably 4% to 8% is suitable. 35
- Examples of oils suitable for inclusion in the present compositions include:-  
 mineral oils, vegetable oils, synthetic fatty acid esters, fatty alcohols, lanolin and its derivatives.
- Examples on non-ionic emulsifiers suitable for inclusion in the present compositions include:-  
 40 sorbitan monostearate, glyceryl monostearate, polysorbates, polyethylene derivatives of fatty alcohols. 40
- The compositions of this invention should desirably include an anti-oxidant effective in preventing oxidation of the retinol acetate and consequent reduction in the activity of the composition. Some anti-oxidants are effective in this respect but themselves oxidise to give a  
 45 noticeable yellowing of the cream. 45
- Two anti-oxidants which are particularly suitable for incorporation are butylated hydroxytoluene (BHT), correct chemical name 2,6-di-tert-butyl-p-cresol and butylated hydroxyanisole (BHA), correct chemical name 2-tert-butyl-4-hydroxyanisole or 3-tert-butyl-4-hydroxyanisole or a mixture of these. Accordingly in another of its aspects, the invention includes a composition in  
 50 accordance with the invention including BHT and/or BHA as anti-oxidant. 50
- The retinol acetate component of the compositions is preferably dispersed in the emulsion in the form of a "solubilised" mixture. Such mixtures are generally solutions of retinol acetate in hydrophilic organic solvents such as glycerine and/or propylene glycol, together with a surfactant such as "Tween 80".
- 55 The following is an example of a composition in accordance with the invention: 55

BEST AVAILABLE COPY

FORMULA		% w/w	
5	Arlacel 60 (Sorbitan Stearate)	2.00	5
	Tween 60 (Polysorbate 60)	2.00	
	Cetyl alcohol	2.00	
	Emulgade F (Emulsifying Wax)	2.50	
	Mineral Oil	25.00	
10	Lanolin	2.50	10
	Cetiol V (Decyl Oleate)	2.00	
	Preservatives	0.37	
	Anti-oxidant (BHT)	0.20	
	Perfume	0.45	
15	Water soluble retinol acetate*	3,000–7,000 IUg <sup>-1</sup>	15
	Deionised water	to 100.00	
20	*Retinol acetate 1 × 10 <sup>6</sup> IUg <sup>-1</sup>	10.00	20
	Tween 80 ("Tween" is a Registered Trade Mark)	50.00	
	Glycerine	15.00	
	Propylene glycol	15.00	
25	Water	to 100.00	25

#### CLAIMS

1. A skin-care composition comprising an oil-in-water emulsion base comprising from 20 to 40% by weight of oil, a non-ionic emulsifying agent in an amount greater than 1% by weight and retinol acetate in an amount from 1,000 to 15,000 IUg<sup>-1</sup>.
2. A composition as claimed in claim 1 comprising from 3,000 to 6,900 IUg<sup>-1</sup> retinol acetate.
3. A composition as claimed in claim 1 or claim 2 comprising from 2 to 12% by weight of non-ionic emulsifying agent.
4. A composition as claimed in claim 1 or claim 2 comprising from 4 to 8% by weight of non-ionic emulsifying agent.
5. A composition as claimed in any one of the preceding claims wherein the oil is selected from mineral oil, vegetable oil, synthetic fatty acid esters, fatty alcohols, or lanolin or its derivatives.
6. A composition as claimed in any one of the preceding claims wherein the non-ionic emulsifier is selected from sorbitan monostearate, glyceryl monostearate, polysorbates and polyethylene derivatives of fatty alcohols.
7. A composition as claimed in any one of the preceding claims which includes butylated hydroxytoluene or butylated hydroxyanisole as an antioxidant.
8. A composition as claimed in any one of the preceding claims wherein the retinol acetate is incorporated as a solution in hydrophilic organic solvents also including a surfactant.
9. A composition as claimed in claim 1, substantially as hereinbefore described in the Example.